

Application No: 10/646,784

Amendment Dated: April 26, 2007

Response to Notice of Non-Compliant Amendment mailed on April 3, 2007

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**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of the Claims:**

1. (CURRENTLY AMENDED) A method of increasing anti-tumor effect of interferon  $\gamma$ , said method comprising administering to a patient in need thereof an effective amount of MIS having the amino acid sequence of SEQ ID NO: 5 or 6 or a fragment thereof, and an effective amount of interferon  $\gamma$ , wherein the effective amount of interferon  $\gamma$  is an amount that results in decreased side effects associated with interferon  $\gamma$  to the patient, thereby increasing anti-tumor effect of interferon  $\gamma$ .
2. (ORIGINAL) The method of claim 1, wherein said patient has primary tumor growth.
3. (ORIGINAL) The method of claim 1, wherein said patient has metastatic tumor growth.
4. (ORIGINAL) The method of claim 1, wherein said patient has a tumor selected from the group consisting of vulvar epidermoid carcinoma, cervical carcinoma, endometrial adenocarcinoma, ovarian adenocarcinoma, and ocular melanoma.
5. (ORIGINAL) The method of claim 1, wherein said patient has a tumor selected from the group consisting of prostate, lymphoid, breast, cutaneous and germ cell tumors.
6. (CURRENTLY AMENDED) The method of claim 1, wherein said MIS or a fragment thereof has a molecular weight of 140 kDa or 70 kDa.
7. (CURRENTLY AMENDED) The method of claim 6, wherein said MIS or a fragment thereof is proteolytically cleaved by reacting with a proteolytic compound to form protein fragments having a molecular weight of about 57 kDa and 12.5 kDa.
8. (CURRENTLY AMENDED) The method of claim 1, wherein said MIS or a fragment thereof, is recombinant human MIS (rhMIS). ~~rhMIS~~

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9. (CURRENTLY AMENDED) The method of claim 1, wherein said MIS fragment is a C-terminal fragment of MIS, wherein the C-terminal fragment comprises 108 or more amino acids at the C-terminal, or has amino acid sequence of SEQ ID NO:11.~~substantially free of N-terminal fragment.~~
10. (ORIGINAL) The method of claim 9, wherein said C-terminal fragment of MIS has a molecular weight of about 25 KDa or about 12.5 kDa.
11. (CURRENTLY AMENDED) The method of claim 10, wherein the C-terminal fragment of MIS is derived from recombinant human MIS (rhMIS).~~rhMIS.~~
- 12 - 13. (CANCELLED)
14. (ORIGINAL) The method of claim 1, wherein said interferon is administered in an amount of about  $1 \times 10^1$  to  $1 \times 10^5$  International Units per administration.
15. (ORIGINAL) The method of claim 1, wherein said interferon is administered in an amount of about  $1 \times 10^2$  to  $1 \times 10^5$  International Units per administration.
16. (ORIGINAL) The method of claim 1, wherein said interferon is administered in an amount of about  $1 \times 10^3$  to  $1 \times 10^5$  International Units per administration.
17. (ORIGINAL) The method of claim 1, wherein said interferon is administered in an amount of less than  $1 \times 10^6$  International Units per administration.
18. (CURRENTLY AMENDED) A method of inhibiting growth of tumor, said method comprising administering to a patient an effective amount of MIS having the amino acid sequence of SEQ ID NO: 5 or 6 or a fragment thereof, and an effective amount of interferon  $\gamma$ , wherein the effective amount of interferon  $\gamma$  is the amount that results in decreased side-effects associated with interferon  $\gamma$  to the patient.
19. (ORIGINAL) The method of claim 18, wherein said patient has primary tumor growth.
20. (ORIGINAL) The method of claim 18, wherein said patient has metastatic tumor growth.

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21. (ORIGINAL) The method of claim 18, wherein said patient has a tumor selected from the group consisting of vulvar epidermoid carcinoma, cervical carcinoma, endometrial adenocarcinoma, ovarian adenocarcinoma, and ocular melanoma.
22. (ORIGINAL) The method of claim 18, wherein said patient has a tumor selected from the group consisting of prostate, lymphoid, breast, cutaneous and germ cell tumors.
23. (ORIGINAL) The method of claim 18, wherein said MIS has a molecular weight of 140 kDa or 70 kDa.
24. (ORIGINAL) The method of claim 23, wherein said MIS is proteolytically cleaved by reacting with a proteolytic compound to form protein fragments having a molecular weight of about 57 kDa and 12.5 kDa.
25. (CURRENTLY AMENDED) The method of claim 18, wherein said MIS is recombinant human MIS (rhMIS) ~~rhMIS~~.
26. (CURRENTLY AMENDED) The method of claim 18, wherein said ~~MIS fragment~~ is a C-terminal fragment of MIS, wherein the C-terminal fragment comprises 108 or more amino acids at the C-terminal, or has amino acid sequence of SEQ ID NO:11 or a fragment thereof, substantially free of N-terminal fragment.
27. (ORIGINAL) The method of claim 26, wherein said C-terminal fragment of MIS has a molecular weight of about 25 kDa or about 12.5 kDa.
28. (CURRENTLY AMENDED) The method of claim 27, wherein the C-terminal fragment of MIS is derived from recombinant human MIS (rhMIS) ~~rhMIS~~.
- 29 - 30. (CANCELLED)
31. (ORIGINAL) The method of claim 18, wherein said interferon is administered in an amount of about  $1 \times 10^1$  to  $1 \times 10^5$  International Units per administration.

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32. (ORIGINAL) The method of claim 18, wherein said interferon is administered in an amount of about  $1 \times 10^2$  to  $1 \times 10^5$  International Units per administration.
33. (ORIGINAL) The method of claim 18, wherein said interferon is administered in an amount of about  $1 \times 10^3$  to  $1 \times 10^5$  International Units per administration.
34. (ORIGINAL) The method of claim 18, wherein said interferon is administered in an amount of less than  $1 \times 10^6$  International Units per administration.
35. (WITHDRAWN) A tumor inhibiting pharmaceutical composition comprising an effective tumor inhibiting amount of MIS and interferon, wherein said effective tumor inhibiting amount of interferon is an amount that results in decreased side effects.

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